

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N-1257]

International Drug Scheduling; Convention on Psychotropic Substances; 4-Bromo-2,5-dimethoxyphenethylamine (2C-B); Gamma-hydroxybutyric acid (GHB); 4-Methylthioamphetamine (4-MTA); N-Methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB); Diazepam (INN); Zolpidem (INN)

AGENCY: Food and Drug Administration, HHS.

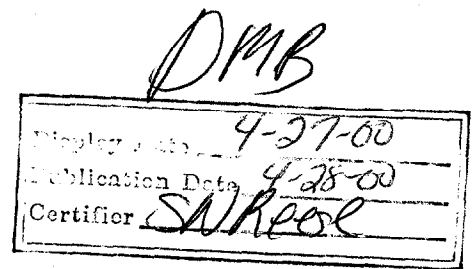
ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is requesting interested persons to submit comments concerning abuse potential, actual abuse, medical usefulness, and trafficking of six drug substances. These comments will be considered in preparing a response from the United States to the World Health Organization (WHO) regarding the abuse liability and diversion of these drugs. WHO will use this information to consider whether to recommend that certain international restrictions be placed on these drugs. This notice requesting comments is required by the Controlled Substances Act (CSA).

DATES: Submit written comments by *[insert date 15 days after date of publication in the Federal Register]*.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Corinne P. Moody, Center for Drug Evaluation and Research (HFD-009), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1999, e-mail: Moody@cder.FDA.gov.



SUPPLEMENTARY INFORMATION: The United States is a party to the 1971 Convention on Psychotropic Substances. Article 2 of the Convention on Psychotropic Substances provides that if a party to the convention or WHO has information about a substance, which in its opinion may require international control or change in such control, it shall so notify the Secretary General of the United Nations and provide the Secretary General of the United Nations with information in support of its opinion.

The CSA (21 U.S.C. 811 *et seq.*) (Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970) provides that when WHO notifies the United States under Article 2 of the Convention on Psychotropic Substances that it has information that may justify adding a drug or other substances to one of the schedules of the convention, transferring a drug or substance from one schedule to another, or deleting it from the schedules, the Secretary of State must transmit the notice to the Secretary of Health and Human Services (the Secretary of HHS). The Secretary of HHS must then publish the notice in the **Federal Register** and provide opportunity for interested persons to submit comments that will be considered by HHS in its preparation of the scientific and medical evaluations of the drug or substance. The Secretary of HHS received the following notices from WHO:

I. WHO Notification

Ref.: C.L.1.2000

WHO questionnaire for collection of information for review of dependence-producing psychoactive substances.

The Director-General of the World Health Organization presents her compliments and has the pleasure of informing Member States that the Thirty-second Expert Committee on Drug Dependence (ECDD) will meet from 11 to 14 September 2000 to review the following substances:

1. 4-Bromo-2,5-dimethoxyphenethylamine (2C-B)
2. Gamma-hydroxybutyric acid (GHB)

3. 4-Methylthioamphetamine (4-MTA)¹
4. *N*-Methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB)
5. Diazepam (INN)
6. Zolpidem (INN)

One of the essential elements of the established review procedure is for the Secretariat to collect relevant information from Member States to prepare a Critical Review document for submission to the Expert Committee on Drug Dependence. The World Health Organization invites Member States to collaborate, as in the past, in this process by providing pertinent information mentioned in the attached questionnaire² concerning the substances listed above.

Further clarification on any of the above items can be obtained from Quality Assurance and Safety: Medicines (QSM), Essential Drugs and Medicines Policy (EDM), WHO, Geneva, to which replies should be sent not later than 1 May 2000.

GENEVA, 12 January 2000

WHO Questionnaire for review of dependence-producing psychoactive substances by the Thirty-second Expert Committee on Drug Dependence.

Substance reported on:

1. Availability of the substance (registered, marketed, dispensed, etc.);
2. Extent of the abuse or misuse³ of the substance;
3. Degree of seriousness of the public health and social problems associated with the abuse of the substance (statistics on cases of overdose deaths, dependence, etc.); and

¹ If the reply to the questionnaire confirms a medical use of 4-MTA recognized by any Member State, the substance will be subjected to a prereview instead of a critical review.

² For Ministries of Health only.

³ In this questionnaire, "abuse or misuse" refers to use of the substance other than for medical or scientific purposes.

4. Any information on the nature and extent of illicit activities involving the substance (clandestine manufacture, smuggling, diversion, seizure, etc.).

In addition to the above, with regard to Diazepam (INN) report on:

5. The impact of transferring diazepam from Schedule IV to Schedule III of the Convention on Psychotropic Substances, 1971, and its effect on availability for medical use.

In addition to items 1 to 4 above, with regard to Zolpidem (INN) report on:

6. The impact of placing zolpidem in Schedule IV of the Convention on Psychotropic Substances, 1971, and its effect on availability for medical use.

II. Background

The substance 4-Bromo-2,5-dimethoxyphenethylamine (2C-B) is a structural analogue of the phenethylamine hallucinogens. In various preclinical and clinical studies, it has been described as a stimulant, depressant, and hallucinogen, but appears to more closely fit the profile of the latter. It is not marketed in the United States, however, it is controlled domestically in Schedule I of the CSA.

Gamma-hydroxybutyric acid (GHB) is a substance classified as a central nervous system depressant. It is not marketed in the United States. The Drug Enforcement Administration published a final rule on March 13, 2000 (65 FR 13235), placing gamma-hydroxybutyric acid and its salts, isomers, and salts of isomers into Schedule I of the CSA under Public Law 106-172. The final rule imposes Schedule III security requirements for registered manufacturers and distributors of GHB when it is manufactured, distributed, or possessed in accordance with FDA authorized investigational new drug exemptions under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)). If drug products containing GHB are approved by FDA, the final rule places FDA approved products containing GHB into Schedule III of the CSA under Public Law 106-172.

The substance 4-Methylthioamphetamine (4-MTA) is a compound structurally similar to amphetamine. 4-MTA is reported to have physiological effects similar to that of 3,4-

methylenedioxyamphetamine (MDA) and 3,4-methylenedioxymethamphetamine (MDMA/ecstasy). The substance is not marketed in the United States. It is not specifically listed as a controlled substance in the United States. However, it is considered a Schedule I controlled substance as an analogue of either MDA or MDMA under the analogue provisions of the CSA.

N-Methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB) is a positional isomer of MDE (3,4-methylenedioxy-*N*-ethylamphetamine) which is controlled domestically in Schedule I. The psychoactive effects of MBDB have been described as hallucinogenic. It is not marketed in the United States. As an isomer of MDE, MBDB is a Schedule I substance in the United States.

Diazepam (INN) is a benzodiazepine derivative. It is marketed in the United States for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety; in acute alcohol withdrawal, it is used in the symptomatic relief of acute agitation, tremor, impending or acute delirium tremens, and hallucinosis; as an adjunct for the relief of skeletal muscle spasm; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; tetanus; as an adjunct in convulsive disorders; and as a premedication for relief of anxiety and tension in patients who are to undergo surgical procedures. Domestically, it is controlled in Schedule IV of the CSA. Diazepam is controlled internationally in Schedule IV of the Psychotropic Convention.

Zolpidem (INN) is a hypnotic agent with a chemical structure unrelated to benzodiazepines, barbiturates, or other drugs with known hypnotic properties. It interacts with a GABA-BZ receptor complex and shares some of the pharmacological properties of the benzodiazepines. It is marketed in the United States for the short-term treatment of insomnia. Domestically, it is controlled in Schedule IV of the CSA.

III. Opportunity to Submit Domestic Information

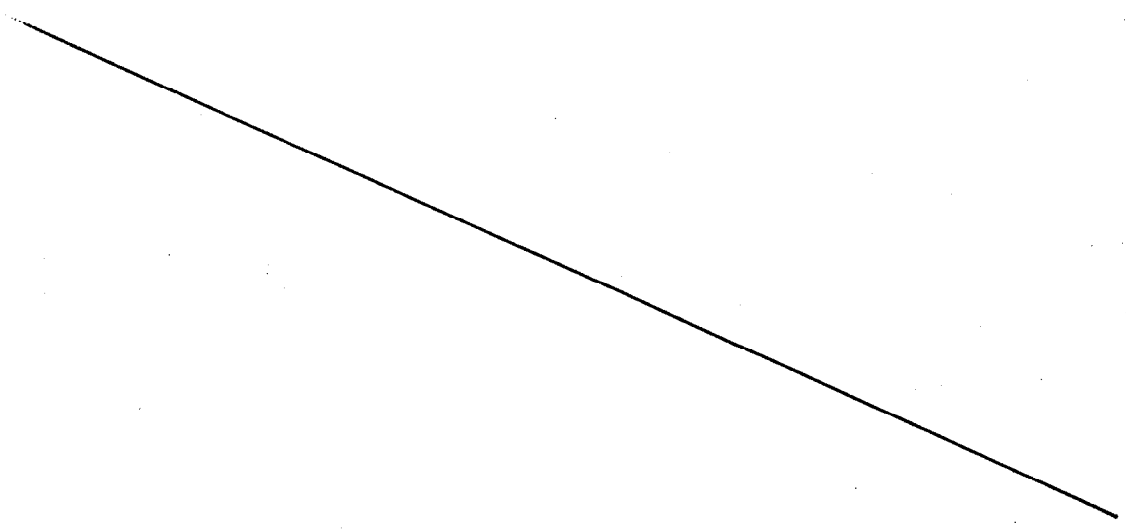
As required by section 201(d)(2)(A) of the CSA (21 U.S.C. 811 (d)(2)(A)), FDA, on behalf of the Department of Health and Human Services (DHHS), invites interested persons to submit comments regarding the six named drugs. Any comments received will be considered by DHHS when it prepares a scientific and medical evaluation of these drugs. DHHS will forward a scientific

and medical evaluation of these drugs to WHO, through the Secretary of State, for WHO's consideration in deciding whether to recommend international control/decontrol of any of these drugs. Such control could limit, among other things, the manufacture and distribution (import/export) of these drugs and could impose certain recordkeeping requirements on them.

DHHS will not now make any recommendations to WHO regarding whether any of these drugs should be subjected to international controls. Instead, DHHS will defer such consideration until WHO has made official recommendations to the Commission on Narcotic Drugs, which are expected to be made in late 2000. Any DHHS position regarding international control of these drugs will be preceded by another **Federal Register** notice soliciting public comments as required by 201(d)(2)(B) of the CSA.

IV. Comments

Interested persons may submit to the Dockets Management Branch (address above) written comments regarding the drugs by *[insert date 15 days after date of publication in the **Federal Register**]*. This abbreviated comment period is necessary to allow sufficient time to prepare and submit the domestic information package by the deadline imposed by WHO. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document.



Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m.,
Monday through Friday.

Dated: 4/24/00

LDC April ~~April~~ 24, 2000



Margaret M. Dotzel
Acting Associate Commissioner for Policy

[FR Doc. 00-???? Filed ??-??-00; 8:45 am]

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